UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte PAUL P. LATTA

Appeal 2007-2397
Application 10/823,263
Technology Center 1600

Decided: October 05, 2007

Before ERIC GRIMES, LORA M. GREEN, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of Claims 1-11, 13, and 14. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF THE CASE

This is an appeal from the Examiner's final rejection of Claims 1-11, 13, and 14, which are all the pending claims in the application at issue in this proceeding (Supp. Appeal Br. 2.[1]). The following rejections are appealed:

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[1] "Supp. Appeal Br." is a reference to the Supplemental Appeal Brief which is date stamped July 25, 2006.

1. Claims 1-4, 6-11, 13, and 14 stand rejected under 35 U.S.C. § 103(a) as obvious over Peck (US 6,703,017 B1, Mar. 9, 2004), Fournier (US 5,425,764, Jun. 20, 1995), and Dinsmore (US 5,629,194, May 13, 1997) in view of Posselt (*Ann. Surg.*, Vol. 214, pp. 363-370 (1991)) (Answer 4).

2. Claim 5 stands rejected under 35 U.S.C. § 103(a) as obvious over Peck, Fournier, and Dinsmore in view of Posselt as applied to claims 1-4, 6-11, 13, and 14, further in view of Hubbell (US 5,529,914, Jun. 25, 1996) (Answer 7).

Claim 1 is the only independent claim on appeal. We select claim 1 as representative of the claimed subject matter. Claim 1 reads as follows:

> 1. A method of treating diabetes in a mammal in need thereof, comprising the steps of:
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> implanting in said mammal a tolerizing dose of insulin-secreting cells encapsulated in a biologically compatible permselective membrane, wherein said implanting step is subcapsular, subcutaneous, intraperitoneal or intraportal; then
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> administering to said mammal a therapeutic dose of corresponding unencapsulated insulin-secreting cells.

DISCUSSION

The claimed invention

For certain human diseases, organ transplantation is the only alternative to certain death (Specification 1). However, when a foreign donor is utilized as the source as the transplanted organ tissue, the patient's immune system will recognize it as foreign and reject it. To prevent tissue rejection, it is necessary to administer high-risk, "immunosuppressive drugs to keep the immune system from destroying the transplanted organ"

(Specification 1: 19-20). In addition to drugs, the Specification describes several other prior art approaches to prevent organ rejection, including thymus inoculation, irradiation, administering monoclonal antibodies to suppress the immune system, and tissue encapsulation (Specification 2-3).

To address the problem of tissue rejection, the Specification describes "a method of creating immunological tolerance to foreign cells, tissues or organs in a mammal, comprising the step of implanting in the mammal a tolerizing dose of foreign cells or tissue encapsulated in a biologically compatible permselective membrane" (Specification 3). "Antigens shed from the [tolerizing dose of] transplanted cells pass through the permselective membrane into the body of the recipient where they are fully exposed to the immune system. The immune system will recognize these antigens as 'foreign' and destroy them. . . . In time, the immune system will . . . become tolerant of these antigens . . . [and to] that particular cell type from that particular donor" (Specification 8).

Claim 1, which is the only independent claim on appeal, is directed to a two-step method of treating diabetes in a mammal. In the first step, "a tolerizing dose of insulin-secreting cells encapsulated" in a membrane is implanted into a mammal. The claim specifies that the implanting is "subcapsular, subcutaneous, intraperitoneal or intraportal." The second step comprises administering "a therapeutic dose of corresponding unencapsulated insulin-secreting cells." As explained in the Specification, the "tolerizing dose" causes the mammal to become "tolerant" of a subsequent "therapeutic dose" of the same insulin-secreting cells and therefore does not reject the insulin-secreting cells.

The rejections

Claims 1-4, 6-11, 13, and 14 stand rejected under 35 U.S.C. § 103(a) as obvious over Peck, Fournier, or Dinsmore in view of Posselt. Claim 5 stands rejected as obvious over Peck, Fournier, or Dinsmore in view of Posselt, further in view of Hubbell.

The Examiner makes the following findings:

1. Peck, Fournier, and Dinsmore describe treating diabetes in a mammal comprising administering insulin-producing cells encapsulated in biologically compatible membrane (Answer 4-5). *See* Peck, Abstract and at cols. 6, 8, 9-14, and 23 (Example 12); Fournier, Abstract and at cols. 5-6; and Dinsmore, Abstract and at cols. 17-18 (Example II).

2. Posselt "teach[es] that the important goal in the treatment of insulin-dependent diabetes by pancreatic islet transplantation is the development of strategies that allow permanent survival of pancreatic islet without continuous host immunosuppression" (Answer 5). *See* Posselt, at 363 ("The failure of currently available immunosuppressive protocols to prolong the survival of pancreatic islet allografts[2] has prompted a search for alternate methods that can permit long-term graft function without the need for chronic immunosuppression").

3. Posselt "further teach[es] a strategy comprising [a] two step process: first administering a small dose of cells that induces an unresponsive state, i.e. tolerizing dose and then administering [a] fully therapeutic dose, at another site" which "permits the survival of [the] pancreatic islet transplant" (Answer 5). *See* Posselt, Abstract.

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[2] An "allograft" is tissue from the same species, but from a non-identical individual.

Based on these findings, the Examiner concludes that it would have been obvious to one of ordinary skill in the art to have administered a tolerizing dose as taught by Posselt in the method of treating diabetes comprising implanting pancreatic islet cells as described in Peck, Fournier, or Dinsmore because Posselt teaches that a tolerizing dose of pancreatic cells permits the subsequent survival of pancreatic cell transplants (Answer 6).

Analysis

In making an obviousness determination over a combination of prior art references, it is important to identify a reason why persons of ordinary skill in the art would have attempted to make the claimed subject matter. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007).

Here, the Examiner contends that Posselt's teaching that a tolerizing dose of pancreatic cells permits survival of subsequent pancreatic cell transplants would have prompted persons of skill in the art to have modified the prior art to have made the claimed method of treating diabetes in a mammal.

Appellant contends that persons skilled in the art would not have had reason to make the claimed treatment method. Appellant asserts that Posselt does not describe implanting a tolerizing dose of insulin-secreting cells which is "subcapsular, subcutaneous, intraperitoneal or intraportal" as recited in claim 1 (Supp. Appeal Br. 8). Appellant urges that he "was the first one to teach that implantation of insulin-producing cells in sites other than thymus produces tolerance to the implanted cells. . . . Contrary to the Examiner's statement, the instant method as claimed in the present Claims

1-14 specifies the non-thymus implantation sites for the tolerizing dose of encapsulated cells. This limitation is not suggested in any of the cited references. Therefore, the cited references fail to suggest the claimed method" (Supp. Appeal Br. 8).

We agree with Appellant and reverse the rejection. Posselt teaches that "pancreatic islet allografts transplanted to the thymus of rats . . . induce specific unresponsiveness[3] to subsequent extrathymic transplants" (Posselt, Abstract). Posselt transplanted pancreatic islet cells directly into the *thymus* gland of rats (Posselt, at 365). With respect to Claim 1, thymic transplantation would correspond to the claimed step of "implanting . . . a tolerizing dose of insulin-secreting cells." These same rats received a subsequent islet allograft transplanted intraportally into the liver (Posselt, at 365). The latter step corresponds to the second step of Claim 1 in which a "therapeutic dose" is administered to mammals.

To test the efficacy of the second intraportal transplant, the thymic allograft was removed (Posselt, at 365). Posselt showed that the rats remained normoglycemic, indicating that the islet cells in the portal islet transplant remained functional (*id.*). "In fact in none of the 11 acutely diabetic BB rats transplanted with Lewis islets was there ever an indication from blood glucose values or histology that even mild rejection or autoimmune insulitis occurred" (Posselt, at 369, cols. 1-2).

In contrast to this success, Posselt reports that a first allograft transplanted into other regions of the rat did not induce "unresponsiveness"

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[3] "Unresponsiveness" refers to the same condition as "tolerance." When a mammal is *unresponsive* to a cell or tissue, it does not immunologically reject it; it *tolerates* its presence in the body.

to subsequent grafts as did the thymic allografts. Posselt describes an experiment involving rats who received a first kidney subcapsular allograft transplant that maintained function (Posselt, at 367, col. 1). These animals allowed Posselt to "assess the capacity of allografts in this site [i.e., subcapsular] to induce unresponsiveness" to subsequent transplants (*id.*). In one animal who received a second islet transplant intraportally into the liver, "only a few recognizable islets remained in the liver . . . [I]t appeared that the persistence of allogenic islets in the kidney does not diminish the vigor of the immune response to subsequent allografts of . . . extrathymic islets" (*id.*). Therefore, only grafts into the thymus produced unresponsiveness to subsequent grafts into other parts of the body.

Thus, we concur with Appellant that Posselt teaches away from the claimed invention. A reference teaches away "when a person of ordinary skill, upon examining the reference, would be discouraged from following the path set out in the reference, or would be led in a direction different from the path that was taken by the applicant. . . . [I]n general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). In this case, Posselt teaches away from the claimed step of "implanting . . . a tolerizing does of insulin-secreting cell . . . wherein the implanting step is subcapsular, subcutaneous, intraperitoneal or intraportal" because Posselt showed that subcapsular tolerization failed and that thymic transplantation was necessary to achieve unresponsiveness to subsequent grafts. *See* Supp. Appeal Br. 8: 1-9. Therefore, a skilled worker would not have expected that tolerization at extrathymic sites as claimed ("subcapsular,

subcutaneous, intraperitoneal or intraportal") would be an effective step in a method treating diabetes and would have been led away from trying it.

The Examiner asserts, without explanation, that "subcapsular, subcutaneous, intraperitoneal or intraportal" does not exclude implanting tolerizing cells into the thymus (Answer 12). We do not agree. None of these recited routes involve thymus transplantation. Thus, we find the Examiner's interpretation of "subcapsular, subcutaneous, intraperitoneal or intraportal" to include intrathymic implantation to be an improper interpretation of the scope of Claim 1.

For the foregoing reasons, we reverse the rejection of Claims 1-4, 6-11, 13, and 14. We also reverse the rejection of Claim 5 because it is based on the same combination of references (Answer 7).

REVERSED

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